

CLAIMS

What is claimed is:

- Subt B1
- 5 1. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor.
- 10 2. An antibody or antigen-binding fragment according to Claim 1 wherein said antibody or antigen-binding fragment thereof inhibits one or more functions associated with binding of the ligand to the receptor.
- 15 3. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the mammalian CC-chemokine receptor 2 is a human CC-chemokine receptor 2.
4. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the antibody or fragment thereof binds the amino-terminal domain or portion thereof of mammalian CC-chemokine receptor 2.
- 20 5. An antibody or antigen-binding fragment thereof according to Claim 4 wherein the portion of the amino-terminal domain is from about amino acid 1 to about amino acid 30.
- 25 6. An antibody or antigen-binding fragment thereof according to Claim 1 wherein the antibody is selected from the group consisting of:
a) monoclonal antibody 1D9;
- 65

7. An antibody or antigen-binding fragment thereof
according to Claim 1 wherein the ligand is a
15 chemokine.

8. ~~An antibody or antigen-binding fragment thereof according to Claim 7 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.~~

- 20 9. The hybridoma cell line deposited under ATCC Accession
No. _____.
10. The hybridoma cell line deposited under ATCC Accession
No. _____.
11. A monoclonal antibody or antigen-binding fragment
25 thereof produced by the hybridoma cell line according
to Claim 9.

12. A monoclonal antibody or antigen-binding fragment thereof produced by the hybridoma cell line according to Claim 10.

13. A test kit for use in detecting the presence of a mammalian CC-chemokine receptor 2 in a biological sample comprising

a) at least one antibody or antigen-binding fragment thereof selected from the group consisting of:

i) monoclonal antibody 1D9;

ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;

iv) monoclonal antibody 8G2;

v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;

vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2; and

vii) antigen-binding fragments of any one of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and

b) one or more ancillary reagents suitable for detecting the presence of a complex between said antibody or antigen-binding fragment thereof and said mammalian CC-chemokine receptor 2 or a portion thereof.

09121784-072200

- 09121781-072306
14. A method of inhibiting the interaction of a cell bearing mammalian CC-chemokine receptor 2 with a ligand thereof, comprising contacting said cell with an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits binding of said ligand to the receptor.
15. A method according to Claim 14 wherein the cell is selected from the group consisting of lymphocytes, monocytes, granulocytes, T cells, basophils, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.
16. A method according to Claim 15 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.
17. A method according to Claim 14 wherein the ligand is a chemokine.
18. A method according to Claim 17 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.
19. A method according to Claim 14 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
 - c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and

d) antigen-binding fragments of any one of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

20. A method of inhibiting HIV infection of a cell,
5 comprising contacting a cell with an effective amount of a composition comprising an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits HIV entry into said cell.

10 21. A method according to Claim 20 wherein the cell is selected from the group consisting of lymphocytes, monocytes, macrophages, granulocytes, T cells, and cells comprising a recombinant nucleic acid encoding CCR2 or a portion thereof.

15 22. A method according to Claim 21 wherein the T cells are selected from the group consisting of CD8+ cells, CD25+ cells, CD4+ cells and CD45RO+ cells.

20 23. A method according to Claim 20 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:

- a) monoclonal antibody 1D9;
b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
c) an antibody which can compete with 1D9 for
25 binding to mammalian CC-chemokine receptor 2; and
d) antigen-binding fragments of any one of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

24. A method of treating HIV in a patient comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits HIV entry into said cell.
25. A method according to Claim 24 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
 - c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and
 - d) antigen-binding fragments of any one of (a) through (c) which binds mammalian CC-chemokine receptor 2 or a portion thereof.
26. A method of detecting expression of mammalian CC-chemokine receptor 2 or portion thereof by a cell, comprising:
- a) contacting a composition comprising a cell to be tested with an antibody or antigen-binding fragment thereof selected from the group consisting of:
 - i) monoclonal antibody 1D9;
 - ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
 - iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;
 - iv) monoclonal antibody 8G2;

09121701-072209

- 5
- 10
- 15
- 20
- 25
- 30
- v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;
- vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;
- vii) antigen-binding fragments of any one of (i) through (vi) which bind mammalian CC-chemokine receptor 2 or a portion thereof; and
- viii) combinations of the foregoing, under conditions appropriate for binding of said antibody or antigen-binding fragment thereof thereto; and
- b) detecting binding of said antibody or antigen-binding fragment thereof, wherein the binding of said antibody or antigen-binding fragment thereof indicates the presence of said receptor or portion of said receptor on said cell.
27. The method of Claim 26 wherein the composition is a sample comprising human cells.
28. A method of detecting a mammalian CC-chemokine receptor 2 or portion of said receptor, comprising:
- a) contacting a sample to be tested with an antibody or antigen-binding fragment thereof which is selected from the group consisting of:
- i) monoclonal antibody 1D9;
- ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

00121784-072300

- iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;
- iv) monoclonal antibody 8G2;
- 5 v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;
- vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;
- 10 vii) antigen-binding fragments of any one of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and
- 15 viii) combinations of the foregoing, under conditions appropriate for binding of said antibody or fragment thereof thereto; and
- b) detecting or measuring binding of said antibody or antigen-binding fragment thereof,
- 20 wherein the binding of said antibody or antigen-binding fragment thereof to material in said sample is indicative of the presence of a mammalian CC-chemokine receptor 2 or portion of said receptor in said sample.
29. A method according to Claim 28, wherein the sample is
- 25 a cellular fraction which, in normal individuals, comprises a mammalian CC-chemokine receptor 2 or portion of said receptor.
30. A method of inhibiting a function associated with binding of a chemokine to a mammalian CC-chemokine receptor 2 or a functional portion of said receptor,
- 30 comprising contacting a composition comprising the receptor or portion with an effective amount of an

00121781:072300

antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody inhibits binding of said chemokine to mammalian CC-chemokine receptor 2 and inhibits one or more functions associated with binding of the ligand to the receptor.

31. A method according to Claim 30 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations thereof.
32. A method according to Claim 30 wherein the antibody or antigen-binding fragment is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;
 - c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and
 - d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.
33. A method of detecting or identifying an agent which binds a mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, comprising combining
- a) an agent to be tested;
 - b) an antibody or antigen-binding fragment selected from the group consisting of:
 - i) monoclonal antibody 1D9;
 - ii) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

09121781-072300

- iii) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2;
- iv) monoclonal antibody 8G2;
- 5 v) an antibody having an epitopic specificity which is the same as or similar to that of 8G2;
- vi) an antibody which can compete with 8G2 for binding to mammalian CC-chemokine receptor 2;
- 10 vii) antigen-binding fragments of any of (i) through (vi) which bind to mammalian CC-chemokine receptor 2 or a portion thereof; and
- 15 viii) combinations of the foregoing; and
- c) a composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof, under conditions suitable for binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof, and detecting or measuring binding of said antibody or antigen-binding fragment to said mammalian CC-chemokine receptor 2 or ligand-binding variant thereof.
- 20
- 25 34. A method according to Claim 33 wherein the formation of a complex between said antibody or antigen-binding fragment and said mammalian CC-chemokine receptor 2 or ligand-binding variant is monitored, and wherein a decrease in the amount of complex formed relative to a
- 30 suitable control is indicative that the agent binds said receptor or ligand-binding variant thereof.

00121781-072308

35. A method according to Claim 33 wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.
36. A method according to Claim 35, wherein the composition comprising a mammalian CC-chemokine receptor 2 or a ligand-binding variant thereof is a membrane fraction of said cell bearing recombinant CC-chemokine receptor 2 or ligand-binding variant thereof.
37. A method according to Claim 33 wherein the antibody or antigen-binding fragment thereof is labeled with a label selected from the group consisting of a radioisotope, spin label, antigen label, enzyme label, fluorescent group and chemiluminescent group.
38. A method according to Claim 33 wherein the agent is an antibody having specificity for a mammalian CC-chemokine receptor 2 or antigen-binding fragment thereof.
39. A method of inhibiting HIV infection in a patient, comprising administering to the patient a composition comprising an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion thereof and inhibits binding of HIV to the receptor or portion thereof.

00121704-072308

- 00121781-072290
40. A method according to Claim 39 wherein the antibody or antigen-binding fragment thereof is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - 5 b) an antibody having an epitopic specificity which is the same as or similar to that of;
 - c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and
 - 10 d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.
41. A method of inhibiting leukocyte trafficking in a patient, comprising administering to the patient a composition comprising an effective amount of an
- 15 antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor and inhibits binding of a ligand to the receptor.
42. A method according to Claim 41 wherein the ligand is a
- 20 chemokine.
43. A method according to Claim 42 wherein the chemokine is selected from the group consisting of MCP-1, MCP-2, MCP-3, MCP-4 and combinations of the foregoing.
44. A method according to Claim 41 wherein the antibody or
- 25 antigen-binding fragment thereof is selected from the group consisting of:
- a) monoclonal antibody 1D9;
 - b) an antibody having an epitopic specificity which is the same as or similar to that of 1D9;

- c) an antibody which can compete with 1D9 for binding to mammalian CC-chemokine receptor 2; and
d) antigen-binding fragments of any of (a) through (c) which bind to mammalian CC-chemokine receptor 2 or a portion thereof.

5

45. A composition comprising an antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and an optional physiologically acceptable vehicle.

10

46. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor with an IC_{50} of less than about 1.0 $\mu\text{g/ml}$.

15

47. An antibody or antigen-binding fragment thereof according to Claim 46 wherein the IC_{50} is less than about 0.05 $\mu\text{g/ml}$.

20

48. An antibody or antigen-binding fragment thereof according to Claim 46 wherein the IC_{50} is less than about 0.05 $\mu\text{g/ml}$.

49. An antibody or antigen-binding fragment thereof which binds to a mammalian CC-chemokine receptor 2 or portion of said receptor, wherein said antibody or antigen-binding fragment thereof inhibits binding of a ligand to the receptor, and wherein the antibody or

25

Subt
B

00121784-072308

antigen-binding fragment binds the receptor with an affinity of at least about 0.1×10^{-9} M.

50. An antibody or antigen-binding fragment thereof according to Claim 49, wherein the affinity is at least about 1×10^{-9} M.

51. An antibody or antigen-binding fragment thereof according to Claim 50, wherein the affinity is at least about 3×10^{-9} M.

52. A method of treating a CC-chemokine receptor 2-mediated disorder in a patient, comprising administering to the patient an effective amount of an antibody or antigen-binding fragment thereof which binds to mammalian CC-chemokine receptor 2 or portion thereof.

Subt
B5
10
001-072298

add
B6

Add
D1

add
E6